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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,388	11/21/2001	Wataru Morikawa	MORIKAWA4A	1349

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EXAMINER
HARRIS, ALANA M

ART UNIT	PAPER NUMBER
1642	5

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,388	MORIKAWA ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Upon reconsideration the Examiner has rejoined Group I (claims 1 and 4) and Group II (claims 2 and 3) of the election/restriction requirement mailed April 25, 2003. Accordingly, all claims will be examined.

2. Claims 1-4 are pending.

Claims 1-4 are examined on the merits.

Specification

3. The disclosure is objected to because of the following informalities: on page 22, line 22 the recitation "dived" should be replaced with the term "divided".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth human plasminogen and not any naturally occurring plasminogen molecule, see Example 7 of page 21. Therefore, the written description is not commensurate in scope with the claims drawn to a naturally occurring plasminogen molecule, which encompasses allelic variants of the said protein, as well as plasminogen molecules from different species (i.e. bovine, porcine, etc).

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

Reiger et al. (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences is not defined. With the exception of Lys-LBS I, the skilled artisan cannot envision the detailed structure of the

encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for human plasminogen is provided in the specification on page 21, Example 7 where the preparation of human plasminogen fragment is presented. However, no disclosure, beyond the mere mention of human plasminogen is made in the specification and that molecule is not identified by a sequence identifier. This is insufficient to support the generic claims as provided by the Interim Written Description

Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore Applicants have only presented evidence of possession of a human plasminogen molecule, but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph.

6. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition for inhibiting lung tumor metastasis and lung tumor growth, does not reasonably provide enablement for a composition for inhibiting any and all tumor metastasis and any and all tumor growth. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants have set forth data that supports the inhibition of lung cancer metastasis and growth, as well as the inhibitory effects of fractions with heparin binding activity on lung tumor metastasis and growth, see Examples 7, 8 and 9, pages 21-23 corresponding to Figure 7 and 8; Example 10, page 24 corresponding to Figure 9. However, the breadth of the claims encompasses the broad treatment of tumor metastasis and tumor growth and the specification is insufficient to enable one of skill in the art to practice the invention absent an undue amount of experimentation. Some of the considerations in determining what constitutes undue experimentation have been summarized as follows: (1) the amount of direction or guidance presented; (2) the presence or absence of working examples; (3) the breadth of the claims; (4) the state of

the prior art; (5) the predictability or unpredictability of the art. *Ex parte Formal, et al.*, 230 USPQ 546 (BPAI, 1986).

As set forth in IDS document, AG the potential for using agents, such as cytokines and antibodies in cancer therapy is great, but clinical results to date have not met the high expectation extrapolated from carefully planned and performed preclinical studies, see bridging paragraph of pages 1079 and 1080. Well-established cancer agents must overcome the physiological barriers to penetrate tumor tissue, effective in *in vivo* microenvironment of solid tumors and reach the target cells *in vivo* in effective quantities with minimal toxicity to normal tissues, see first full paragraph of column 1, page 1080. Applicants claimed cancer agents has not established a sufficient precedent in treatment of a variety of tumors. Applicants have provided data that supports the administration of an effective dose of Lys-LBS-I to immunodeficient mice, however one cannot extrapolate the results based upon one type of tumor to all tumor types. "Even with the best animal model, however, we still need to better understand how the process of biodistribution of various agents "scales-up" from mouse to human.", see column 2 on page 1080.

The selection and development of such therapeutics is art known to be highly unpredictable. The specification exemplifies no examples of the effective use of any composition consisting of Kringles 1 to Kringle 3 of a naturally occurring plasminogen other than the human Lys-LBS I fragment of human plasminogen as a therapeutic pharmacological agent. Therefore, due to the unpredictability of therapeutics and the absence of any evidence concerning the effectiveness of the broadly claimed

composition as a pharmacological agent, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use with a reasonable expectation of success, the invention commensurate in scope with this claim. Additionally, it would require undue experimentation of one skilled in the art to apply a method of treatment to a human based on the teachings of a method of treating a non-human animal.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1 is vague and indefinite in the recitation "binds intensely". It is not clear what is deemed intense, how that intensity is measured and what molecules the comparison is based upon. Accordingly, the metes and bounds cannot be determined.

b. Claim 1 is vague and indefinite in the recitation "non-physiological conditions" and "physiological conditions". The claims do not exemplify or define the said conditions and the metes and bounds of the claim cannot be determined.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is

(703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alana M. Harris, Ph.D.
July 14, 2003